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Transplanting the womb: an examination of the ethics and potential of uterine transplantation

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Transplanting the Womb:

An Examination of the Ethics and Potential of Uterine Transplantation

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Introduction

This thesis serves to explain what a uterine transplant (UTx) is and how may fit into society and pre-existing medical systems. Uterine transplantation (the act of surgically transplanting a donor uterus into a person who lacks one) is currently in the clinical trial stage in several countries around the world and, as with any new medical technology, it is important to pinpoint and examine the bioethical complexities associated with the procedure. Before uterine transplants become more accessible, it is necessary to determine who will be helped by this procedure and to ensure that UTx offers more benefits than risks. This thesis will strive to assess the ethicality of this medical innovation, as well as the societal motivations that have led to its development. I will also investigate how the implementation of uterine transplantation in the medical sphere will change and expand in the future.

In Chapter 1, I intend to briefly outline the history of this procedure and the groups that could benefit from this burgeoning technology. This chapter will also include a brief description of how the procedure works, and an outline of the steps leading up to the human clinical trial stage.

When discussing any new medical procedure it is necessary to examine its bioethical implications and to perform risk-benefit analyses. Chapter 2 will largely be dedicated to this task. This chapter will also discuss the other Assisted Reproductive Technologies (ARTs) that are currently available to help intended parents conceive. Here I will place UTx in conversation with traditional IVF as well as gestational surrogacy.

Chapter 3 will take on the important task of identifying pre-existing procedures and technologies (colloquially termed "quality-of-life procedures") that may supply context and create precedents for this type of medical innovation. Additionally, through the scrutiny of the varied motivations pushing patients toward quality-of-life procedures I wish to demonstrate how societal pressures inform the techniques and procedures that are sought out by patients and subsequently approved by the medical community.

Once these other issues are fully fleshed out, Chapter 4 shall explore the future of uterine transplantation. I will explore how UTx may be aided in the future by other scientific advancements, like 3D bioprinting. Additionally, I will discuss how uterine transplants might one day become available to patients other than cis-women (ie. trans women, cis-men, etc), which might further revolutionize human reproduction.

I will finish this thesis by reiterating my main points and summarizing my conclusions. By critically examining the bioethical risks of uterine transplantation in this thesis I do not intend to discourage the progression of clinical trials and research into the UTx procedure. Instead, I simply aim to raise awareness of all ethical considerations associated with uterine transplantation, and contemplate a future involving UTx.

Chapter 1

Uterine Transplants: Past and Present Applications

In Germany, in 1931, the transgender woman Lili Elbe became the world's first uterine transplant recipient. Three months later, Elbe died from paralysis of the heart due to organ rejection. Though interest in uterine transplants persisted, and studies were conducted to discover anti-rejection medications that would one day make these transplants possible, it was a long time (almost 70 years) before another patient underwent the procedure that ultimately ended Elbe's life. Today, 85 years after her death, uterine transplants are finally gaining mainstream attention from the medical and scientific fields, but many members of the general public still have no idea what they are or what they could mean for societal and medical advancement.

According to the Hastings Center, a preeminent bioethics research institute, a uterine transplant is an experimental procedure developed to enable women without uteri, or with malformed or badly damaged uteri, to become pregnant. This operation involves transplanting a uterus from a living or deceased donor to a recipient (Hastings Center). While this definition is limited, due to its gender-based language and lack of procedural descriptions, it does offer a starting point for understanding uterine transplantation as a concept. Generally, 'women' are considered to be individuals with internal female reproductive organs (a vagina, a uterus, Fallopian tubes, and ovaries), but in actuality many people who identify as women are born without one or all of these organs. The current research on uterine transplants focuses on female-bodied individuals (with two X-chromosomes) who

were either born without uteri or who have had their uteri removed due to medical complications. Keeping this focus in mind, for the majority of this thesis I will refer to people with uteri, and individuals desiring uterine transplants, as "women" and use the pronouns she, her, and hers to address them. The final chapter of this thesis will address the future of uterine transplants, and it is there that I will take the time to discuss the potential influence of uterine transplants in the trans and nonbinary communities.

During the intervening time between the first and second attempts at uterine transplants, medical professionals and scientists did not forget about fertility issues, but instead shifted their focus to other assisted reproductive technologies (ARTs). It was throughout this time that In Vitro Fertilization (IVF) was developed. In Vitro Fertilization is a process where mature eggs are retrieved (either from the intended mother's ovaries or from a donor's ovaries) and fertilized by sperm in a laboratory (Mayo Clinic). The fertilized eggs (embryos) are then implanted into the uterus of a gestational carrier, who could either be the intended mother or a chosen surrogate. While IVF is one of the most widespread ARTs, it still requires a functional uterus, and therefore does not eliminate the perceived "need" for uterine transplants.

Though I have mentioned a shift in focus from UTx to IVF, it would be incorrect to claim that research into uterine transplantation entirely halted during this time. UTx research was still conducted in certain laboratories, but the subjects were not human. During the time before modern research into uterine transplants reached the stage of human clinical trials, many different animal trials were conducted throughout the world, and some are still ongoing. The three main types of animals

that have been involved in these studies are rodents (rats and mice), large domestic species (sheep and pigs) and, most recently, nonhuman primates, including baboons and macaques. Rodent studies were used to develop the basic procedure for uterine transplants that was adopted and greatly altered for use in sheep and pig studies. These animal models were very important for identifying the different potentially harmful events that could cause transplants to be unsuccessful, and analyzing each event separately. These events include surgery at organ recovery, ischemia-reperfusion damage, surgery at transplantation, rejection, and effects of immunosuppressive medication. By isolating each event through the use of control groups, researchers were able to determine how to best mitigate these dangers.

An important contribution from animal trials to UTx is the enhanced knowledge about antirejection drugs that have made allogeneic transplants and transplants from dead donors possible (Brännström 1270-71). Rodent trials tested the efficacy of Cyclosporine as immunotherapy against allograft rejection, and found that while the drug was able to partially suppress rejection of the transplanted uterus, it did not reduce the morphological and histological signs of graft rejection enough to allow for long-term graft survival (Wranning 378). Later trials in rats showed that tacrolimus monotherapy is capable of suppressing rejection of an allotransplanted uterus (Akhi 682). These trials helped to determine the medical regimen for human subjects.

Now that this research has moved into the realm of human trials, it is important to examine the composition of the pool of potential recipients. 1 in 4,500 newborn females are born with Mayer-Rokitansky-Küster-Hauser syndrome, a congenital

disorder that mainly affects the reproductive system and causes the vagina and uterus to be underdeveloped or absent (U.S National Library of Medicine). Individuals with MRKH make up a sizeable portion of uterine transplant candidates, but there are many other medical conditions that lead to dysfunctional uteri. Two common acquired etiologies that make uteri incapable of gestating include fibroids and intrauterine adhesions. Additionally, many women are forced to have hysterectomies due to uterine cancer, excessively heavy periods, endometriosis and a variety of other medical issues. Absolute uterine factor infertility (UFI) is the term used to encompass all causes of female infertility that stem from the anatomical or physiological inability of a uterus to sustain gestation (Lefkowitz et al. 439). It is estimated that throughout the world uterine factor infertility affects 3–5% of the female population.

The likelihood of a woman being deemed "in need" of a uterine transplant correlates with the severity of her conditions. Subjects who have been labeled 100% infertile are more likely to be candidates for clinical trials than those who only have a decreased level of fertility. That being said, women in any of these categories could, in the very near future, find themselves on waiting lists for transplanted uteri.

It is important to note that while some of the aforementioned medical conditions themselves can be life threatening, the absence of a functional uterus, or any uterus at all, is not harmful to a person's health. Therefore, the motivations for research into uterine transplants and the desire, held by some women, to undergo uterine transplantation come from a realm outside of the preservation of life. It is

also clear that the sole motivation for these procedures is not simply to allow interested parties to become parents because other avenues, such as adoption and surrogacy, are available to fulfill that desire. The question of motivation will be fleshed out more thoroughly in later chapters, but it is safe to say that those individuals who are seeking out uterine transplants are doing so because of a strong desire to experience *pregnancy* and give birth to a child.

Almost seven decades after the first uterine transplant was performed, on April 6, 2000 doctors in Saudi Arabia performed a uterine transplant surgery, transferring a healthy uterus from a 46-year-old living donor to a 26-year-old recipient who had previously undergone a hysterectomy. The doctors who conducted this transplant were aware that no successful human uterine transplant had ever been done, and with that in mind they ran an animal study. The study involved transplantation in 16 female baboons and 2 female goats, and produced varied results. The researchers used the information gained from the animal research to structure their human "trial" which consisted of only one patient. The researchers developed their own surgical techniques and immunosuppression regimen and went forward with what they considered to be the first actual human uterine transplant. After 99 days the recipient experienced "a sudden feeling of heaviness, with a foul-smelling vaginal discharge on straining" (Fageeh 249-250) and after diagnosing the patient with a mechanical occlusion of the uterine vessels (which resulted in a uterine infarction) the doctors removed the transplant. Though the donor and recipient both survived the surgeries, practically no medical professionals consider this to be the first

successful uterus transplant, because the uterus was removed before completing its stated purpose of gestating a fetus.

In 2011, another attempt was made at uterine transplantation, this time using a uterus from deceased donor. Doctors in Turkey transplanted the uterus of a 22-year-old brain-dead woman into a 21-year-old woman with congenital uterovaginal agenesis (MRKH). The recipient was selected out of a group of 10 candidates, all with the same congenital disorder, due to her age, health, and the fact that her blood type matched that of the donor. As the recipient had fully functional ovaries, she underwent two cycles of IVF, resulting in eight embryos which were to be stored until the uterine transplant was performed and the recipient had fully healed. The transplant was performed successfully and twenty days after the procedure the patient had her first menstrual cycle. Three months after the transplant she was able to resume sexual activity. At the intervals of four months and six months post-transplantation the recipient had urinary tract infections, but both infections were successfully treated by medication and there was no cause for the removal of the transplant (Ozkan et al.).

The recipient of the 2011 Turkish uterus transplant was the first uterine transplant recipient in history to become pregnant. Almost two years after the initial transplant surgery it was announced that the recipient was pregnant, but eight weeks later, during a routine checkup, the fetal heartbeat could not be detected and the pregnancy was terminated. While doctors stated that the patient would resume IVF treatments once she was “ready”, there is no evidence that IVF was ever resumed and the uterus was eventually removed. This transplant was, in a

way, successful because there was no necrosis of the uterus or other obvious signs of rejection that necessitated immediate removal. While the researchers boast that this was the "first clinical pregnancy in a patient with absolute uterine infertility" (Ozkan et al), the procedure itself is largely considered unsuccessful because it did not result in the birth of a child.

It was not until 2014, when a participant in a Swedish clinical trial gave birth to a healthy male baby, that the medical community could finally cite a successful uterine transplant. The transplant procedure itself was performed in 2013, when a 35 year-old patient with MRKH (Emelie Eriksson) received a uterus from a 61 year-old donor (her mother Marie), who had previously given birth on more than one occasion. The donor and recipient underwent the transplantation procedures at Sahlgrenska University Hospital in Gothenburg, Sweden. One year after the transplant the recipient had her first single embryo transfer (using an embryo created with her oocyte and her husband's sperm), which resulted in pregnancy. In order to stave off rejection, the patient was put on a regimen of triple immunosuppression (tacrolimus, azathioprine, and corticosteroids), which was continued throughout pregnancy. Even though there were multiple episodes of mild rejection (all of which were combatted with corticosteroid treatment) the pregnancy was relatively routine, until the 31st week when the patient was admitted to the hospital with pre-eclampsia. Hours later doctors delivered the baby via caesarean section (Heinonen). A few months after the birth of the child, the transplanted uterus was removed. The removal of the uterus allowed the recipient

to terminate her regimen of immunosuppressant drugs and avoid any long-term side effects associated with these medications.

The Swedish clinical trials used live donors (women who were often genetic relatives of the recipients), resulting in seven successful womb transplants and (as of April 2017) a total of five live births. These trials have proved that uterine transplants are indisputably a viable way to treat uterine factor infertility (though we still don't know the long term effects of UTx on the mothers or the babies). Since the study in Gothenburg, two different clinical trials have gotten underway in the United States, one at the Cleveland Clinic in Cleveland, Ohio, and the other at the Baylor University Medical Center in Dallas, Texas. Two other American clinics have registered for pilot trials, have been approved by UNOS, and may proceed to the clinical trial stage in due course. There have also been attempts in China (November, 2015) and in the Czech Republic (April, 2016). In January 2017 a medical team from Keio University in Japan applied to the university's ethics panel for approval to begin offering uterine transplants. Worldwide, more than 15 uterine transplants have been performed, but so far only the Swedish trials have been deemed *successful* and have resulted in live births (Maron, Donated Uterus).

On February 24, 2016 the surgical team at the Cleveland Clinic performed America's first uterine transplant. Screening for participants began in September of 2015, and the preferred demographic included women aged 21-to-39 with UFI. These women were all required to be in stable romantic relationships, they were required to show that they had enough money to fund their travel and living expenses (Grady). After multiple rounds of medical and psychological evaluations,

a panel of experts chose ten women to participate in the trial. The donors in this trial were all deceased and fell between the ages of 18 and 40 years old. The first participant in the trial to undergo the transplantation process, 26-year-old Lindsey McFarland, experienced a successful procedure. While she and the surgeons were all extremely optimistic about the outcome, McFarland only had her transplanted uterus for a couple of weeks before it was removed, on March 8, 2016, due to a fungal infection that compromised blood supply to the organ (Zeltner). The clinical trial was temporarily put on hold (as of April 2017 the trial is still suspended) while the team modifies the protocol in an attempt to reduce the risk of this complication occurring with the other nine transplants.

Though the Cleveland Clinic trials stalled after the first failed transplant, the Baylor clinical trial is currently ongoing. After a two-year research initiative, in September of 2016 a surgical team at the Baylor University Medical Center performed four uterine transplants (using live "altruistic" donors). In addition to the use of live donors, the Baylor clinic is also using a robot to assist in the removal of the uterus from the donor, which shortens the time in surgery. While three of these transplants quickly failed and required uterine removal, the uterus in the fourth patient (as of April 2017) is still viable. These first four transplants are a part of a larger clinical trial of ten women between the ages of 20 and 35 years old, all of whom were born with MRKH (Goodman).

Animal trials, specifically those done with nonhuman primates as their test subjects have helped to determine the currently accepted transplantation procedure and it's accompanying medications. All three of the modern uterine transplant

clinical trials work off of the same transplant procedural template that was developed based on research with these animal models. A graphic of this procedure in humans is available in Appendix A. Uterine transplantation is a multiple surgery process and it entails the removal of the donor uterus through the isolation of the uterus with bilateral, long venous, and arterial vascular pedicles, the transplantation of the uterus into the recipient and then (after one or two successful pregnancies) an eventual second surgery to remove the transplanted uterus. After the transplanted uterus is removed, it becomes biomedical waste and cannot be used for a subsequent transplant recipient. These procedures have regimented schedules of antirejection medications that are associated with them, which usually include a combination of several different medications at varying doses depending on the stage of the procedure (before, during, and after surgery, as well as different phases of a resulting pregnancy).

Chapter 2

Bioethical Considerations of Uterine Transplants and other ARTs

Uterine transplantation requires the examination of a plethora of different bioethical standards, as it involves several medical topics that often incite bioethical debate: assisted reproductive technologies, transplant surgeries, and elective procedures (which will be addressed more fully in Chapter 3). In addition to the preexisting controversies in all of the aforementioned fields, the uterine transplant is a markedly unique procedure, and therefore has garnered critiques and bioethical questions that are new and UTx-specific. While the concept of a uterine transplant has been considered for many decades, and successful transplants have recently been conducted, the ethical issues are so elaborate, that most western medical associations are being slow to accept the procedure. Even in cases where UTx has been approved and studied, the development of a procedural layout was an arduous process. Dr. Alan Lichtin, of the Cleveland Clinic, said in an interview for the New York Times, that it took about a year of going back and forth before the research team could finally produce a plan that the Cleveland Clinic's 15-member ethics board would approve (Grady).

Assisted reproductive technologies, in general, have long been under fire by those individuals and organizations that believe science should not interfere with conception (mainly members of the religious right). A main ART that faces bioethical scrutiny is In Vitro Fertilization. IVF is often used for another very controversial ART (gestational surrogacy) and is always required in order for uterine transplant recipients to conceive.

Since 1978, when the first IVF baby was born, this procedure has become very common practice in industrialized countries, where almost 10% of all couples experience fertility problems. There is still fear that this technology might be used in the future for the purposes of cloning or eugenics, but the original concern, that IVF babies would be "different" (developmentally or physically) from naturally conceived babies, has been generally dispelled by data analytics over the past four decades. With that fear out of the way, most concerns about IVF are now less centered on medical issues and tend to focus on religious and social objections, as well as legal policies regulating the use of IVF (Banjeree). When a woman undergoes a cycle of In Vitro Fertilization she is given fertility drugs to stimulate oocyte production. After stimulation multiple eggs are retrieved and fertilized in a laboratory dish. In most cases, while many oocytes are fertilized, not all of them are used. Some are not implanted in the uterus and instead might be frozen for future implantation or are donated for research purposes. Some intended parents even choose to have their excess oocytes buried. Usually several fertilized oocytes, which at this point are considered *embryos*, are implanted in the uterus at once, and if multiple embryos are successful, the parent may elect to terminate one or more of the pregnancies to avoid having a multiple birth.

At this point the question of when life begins comes into play. Those who believe that life begins when the sperm fertilizes the egg consider all embryos to be human lives, and therefore take issue with the termination or the freezing/donation of excess embryos. Since it has been postulated that only one out of every 150 IVF implantations results in a live birth, those who view embryos as alive see IVF as a

great and unnecessary waste of life. For people who believe that life begins at implantation as opposed to fertilization, the amount of perceived death is lessened, but still hard to justify (Banjeree).

Statistics show that babies produced through IVF tend be delivered pre-term and with low birth weights as compared to those who were naturally conceived, but these stats can be skewed by the fact that IVF often produces multiple births, and even twins, triplets, etc. who are conceived naturally experience these issues. However, one cannot deny that the increased likelihood of these complications constitutes added risk incurred through IVF. Members of certain religious groups oppose IVF and other assisted reproductive technologies because they believe that God is the only one who should be able to control conception (Banjeree). If that is the truth, a woman who is infertile due to age, medical complications, or any other factors, is not meant to bear a child.

Many critics of IVF also believe that it should not be an option for doctors or parents to choose to not implant an embryo that is *abnormal* (Katz et al. 1119-1121). During IVF, some parents opt for Preimplantation Genetic Diagnosis (PGD), a process in which doctors remove a cell from an embryo and have it tested for specific genetic conditions, before implanting it in womb of the gestational carrier. Usually if it is determined that the embryo would develop into a child with a negative genetic condition, the parents chose not to implant it. This draws a lot of bioethical criticism from pro-life communities and disability activists, as well as scholars and lay people alike who fear that PGD is a stepping-stone to eugenics (Morse).

Opponents of IVF often argue that if an infertile couple truly wishes to have children, they can pursue adoption or foster parenting. Critics of uterine transplantation also use the existence of these options to argue that UTx is not necessary. When performing online research into UTx, adoption and foster care are consistently listed as alternatives to uterine transplants, and so is gestational surrogacy. If a woman does not have a functional uterus, traditional IVF will not work for her. That said, gestational surrogacy, using an embryo made from the oocyte of the intended mother and sperm from the intended father, provides another avenue for biological children, as long as the intended mother has functional ovaries. While gestational surrogacy can technically be achieved through artificial insemination, the resulting child will genetically be that of the intended father and the surrogate (with no genetic relationship to the intended mother). This system is hardly ever used because it can create emotional and legal issues between the surrogate and the intended parents. Most gestational surrogacy involves the intended mother and father using IVF to create embryos that will then be implanted in the uterus of the gestational surrogate. While surrogacy usually results in a child genetically related to the intended parents, people from many different religious, philosophical and social backgrounds find this system to be largely problematic. Additionally, this practice is not universally accessible, as several countries have legally prohibited all forms of surrogacy (France, Iceland, Italy, Pakistan, Saudi Arabia) and others only allow for altruistic surrogacy (Families Through Surrogacy).

Gestational surrogacy, through the use of IVF, faces all of the same ethical issues that traditional IVF confronts, and is additionally considered by many to be

exploitative and akin to prostitution and human trafficking. Surrogacy gets a lot of support from some pro-women organizations and self-proclaimed feminists, as it is a perfect example of "women helping women", and women taking their reproductive rights into their own hands. Conversely, other pro-women organizations and feminists see surrogacy as further commodification of the female body and rail against a system where the womb can be rented out for a price. Personal liberty advocates also see ethical issues with non-altruistic gestational surrogacy because it highlights the issue of parental "ownership" and raises the question, are the intended parents renting the surrogate's womb and time, or are they paying money to purchase a baby (Morse)?

The critiques about unethical practices in surrogacy are even harsher when it comes to "surrogacy tourism". Many parents from Western countries like the United States elect to have their genetic babies gestated in the wombs of impoverished women in other countries, like India, because the process is much cheaper and has less red tape. The women in these countries who become surrogates usually deal with negative social stigma and only elect to do so because they are desperate for money. These women are connected with intended parents through brokers, who take the majority of the profit, and often times the women (like the surrogates at the Akanksha clinic in Anand) are required to stay in hostels for the full nine moths, eat certain foods and refrain from most of their normal daily tasks, in order to ensure that they don't do anything to jeopardize the health of the child (Bhalla). The surrogates connected with these organizations are not even allowed to spend the night with their husbands or go home to visit their children.

In addition to the aforementioned problems with surrogacy institutions, the potential health risks associated with pregnancy and childbirth are transferred to the surrogate. Therefore, these women are not only getting paid to dedicate a long period of time to this process, but also to put their mental and physical health at risk. The postpartum experience is difficult for many women, and can develop into postpartum depression, and there is no way to predict how a gestational surrogate will deal with these hormonal changes in conjunction with the fact that she will not even have a child to nurse and raise after giving birth. In traditional pregnancies, the bond between mother and growing fetus is constantly discussed and reaffirmed, but gestational surrogates are cautioned to remember that they are only carrying the fetus, and they have no claim to the resulting baby. These women are also often cast aside after delivering the babies, and are not offered post-partum medical care or mental health checkups.

While surrogacy challenges traditional ideas about the significance of the gestational process, many women who desire uterine transplants are willing to take on the discomfort and risk of multiple surgeries precisely because they consider the experience of pregnancy, and the nearly ten-month-long journey of gestation, to be invaluable. When debating the ethics of uterine transplantation, much emphasis is placed on whether these new transplants are "worth the risks" when there already exists an extensive list of options (IVF, surrogacy, adoption, and fostering) that can be employed by intended parents with fertility problems. The counter argument with this view is that, while there are preexisting assisted reproductive technologies that share **one** of the primary results of uterine transplants (having a child), no

other technology currently exists to allow people without functional uteri to become *pregnant* and *experience gestation*.

Uterine transplantation brings together, for the first time, the medical specialties of reproductive medicine and transplant surgery. This intersection ensures that uterine transplants are seeped in the ethical issues of both specialties. Dr. Eric Kodish, the director of the Cleveland Clinic's ethics center, deemed uterine transplantation to be ethically superior to surrogacy, and said that through surrogacy, "You create a class of people who rent their uterus, rent their body, for reproduction. It has some gravity. It possibly exploits poor women." (Grady). While some ethicists believe that uterine transplants may constitute a more ethical path, that is not a universally held stance, and it is obvious that uterine transplants are not without their own ethical issues. UTx specific bioethical concerns stem mainly from the risk of the multiple required surgeries, the post-op emotional strain experienced by the donor and the recipient, the need for immunosuppressant medications before and during gestation, and the questions of where and how donor uteri will be procured. Another key issue is that the pregnancy and childbirth experiences will not entirely align with the traditional experiences, as a UTx recipient will be unable to feel most fetal movements or have a vaginal birth.

Like other solid organ transplants, if the donor is living, the surgical risk will be spread to both the donor and the recipient. For a live uterine donor, the operation is not as simple as a standard hysterectomy (which usually takes around an hour and a half) because it is necessary to remove part of the vagina and other tissue needed to attach the uterus to the recipient. This is also a more complex procedure because

the uterine vessels are wound around the ureters, and the surgeons must carefully separate them in order to retrieve the vessels without causing damage to the fragile ureters. Overall, the uterine retrieval process can take from 7 to 11 hours and all of the work is done in close proximity to other vital organs. The transplant surgery is a slightly shorter process, around five hours. The transplant surgery requires the connection of an artery and a vein on both sides of the uterus to the recipient's blood vessels. The donated uterus will also have part of the donor's vagina attached, and that will be stitched directly onto the recipient's vagina. Supporting tissue attached to the uterus will be sewn into the recipient's pelvis to stabilize the transplant. It is not necessary to connect any of the nerves (Grady).

This is not the end of the surgical procedures though, because as stated earlier, a uterine transplant is temporary, and the donor uterus is supposed to be removed after the recipient has had one or two children. This means that the intended mother will have to go through yet another surgery. A UTx recipient who experiences two successful pregnancies would expect to have a total of four scheduled surgeries during this process. Though each specific surgery is no more dangerous than the average surgery, certain academics, such as Arthur Caplan, Professor of Bioethics at NYU, take issue with the amount of risk that is incurred for a transplant surgery that is not lifesaving. In 2007, Caplan went as far as to state that uterine transplantation fails the clinical equipoise test, because he considers gestational surrogacy, adoption and foster care to be valid alternatives, which provide the same result (parenthood) with far less risk to all parties (Caplan et al. 19-20).

The physical and emotional recovery after the uterine transplant procedure can be very difficult for both the donor and the recipient. Several studies conducted in 2011 by researchers from Pamukkale University showed significant increases in sexual dysfunction and decreases in sexual satisfaction for women posthysterectomy (Sözeri-Varma et al.). Due to the fact that this procedure is irreversible, it is extremely important to ensure that all possible donors are made aware of the risks before committing to the procedure. In addition to the physical changes that may occur posthysterectomy, donors may also experience emotional turmoil due to loss of gender identity or changes in sexuality (Lefkowitz et al 443). While many possible donors may feel that these side-effects are not great enough to stop them from helping another woman achieve the ability to carry a child, these emotional and physical changes can truly affect the quality of their lives, and should not be trivialized.

It is not uncommon for organ transplant recipients to experience identity issues post-transplant (which will be further discussed in Chapter 3). While the body benefits from the donated organ or, in the case of UTx, the transplant allows for new opportunities for the recipient, the recipient might be unable to emotionally bond with the donor organ. This inability to bond can cause personality changes, paranoia, and possibly cause the recipient to desire the removal of the transplant. While there has not been any evidence of this emotional rejection of uterine transplants thus far, if a recipient were to feel significantly detached and disillusioned with the donor uterus, she may run the risk of also being unable to emotionally bond with a child who is gestated in the donor uterus (Lefkowitz et al

443). If the mother lacked an emotional bond with the child, and felt like it did not belong to her, she might be inclined to neglect the baby or cause it harm. If this situation were to occur, it would be damaging to the lives of the mother, the child and other members of the family. This is just one of many reasons that psychological examination is necessary both before and after UTx.

Possibly even more ethically daunting, if a UTx recipient became noncompliant with the anti-rejection medication regimen while still pregnant—resulting in the rejection of the transplant—the gestating fetus would most likely be lost. At this point in time in the United States, pregnant women can be legally prosecuted for unhealthy behaviors that could cause (or have caused) harm to a gestating fetus (Boudreaux). If a uterine transplant recipient were to neglect her medication, resulting in the loss of the donor uterus and the fetus, there is no way to know how the law would handle the situation, but it could go so far as to consider the situation a fetal homicide. It is important to consider both of these possible consequences when performing the risk analysis of uterine transplants.

Another risk to the psychological well-being of the recipient stems from the fact that another person needs to undergo risky and irreversible life-altering surgery in order to help them achieve their goal. Whether this person is a relative of theirs, or an anonymous stranger, there is risk that the guilt or shame of including another person in their reproductive journey could lead to emotional problems. If the donor is involved in the life of the recipient, and subsequently suffers from complications due to the surgery, there could be a large amount of strain of their interpersonal relationship (Lefkowitz et al 443).

Ever since general transplant surgeries (ie. Kidney, liver, etc) became such common practice there has been a lot of research into the negative effects of gestating a fetus while on immunosuppressant medications. Due to all of this research, there is now a deep body of evidence and literature that demonstrates the absence of a statistically significant increase in malformations or disabilities in newborns that were gestated by women in the post-transplant setting of solid organs (Lefkowitz et al. 441). This being said, research has shown that solid organ transplant recipients are at increased risk of a large number of different cancers, due to the immunosuppression medications. Transplant recipients have been shown to acquire non-Hodgkin lymphoma (NHL) and cancers of the lung, kidney, and liver at higher rates than members of the general population. NHL and liver cancer can be caused by Epstein-Barr and chronic infection with the hepatitis B and C viruses, respectively, while lung and kidney cancers are not generally thought to be associated with infection (McLaughlin-Drubin and Munger 12-18). Dr. Tzakis, from the Cleveland Clinic, remarked that thousands of women with kidney and liver transplants have given birth to healthy babies, and while transplant recipient mothers are more likely than others to have pre-eclampsia and smaller babies, it is not known whether those problems are caused by immunosuppressants, or by the original illnesses that necessitated the transplants (Grady).

Though there are clearly some added risks from taking immunosuppressants, reports from the National Transplantation Pregnancy Registry (NTPR) strongly support maintenance of immunosuppression combination therapy regimens during pregnancy, and one can interpret these reports as negating the claim that

immunosuppression drugs required for uterine transplants constitute an unethical risk for the mother and the fetus (Lefkowitz et al 441). While the immunosuppressants are, of course, vital to stave off rejection of the transplanted uterus, the risk of post-implantation rejection must be carefully examined. A very intriguing question was brought up by Dr. Alexander Maskin, from the University of Nebraska, "what happens if there is a fetus in the [transplanted] uterus, and you have to take that uterus out?" (Pondrom, Uterus Transplants 375). Depending on the stage of the pregnancy, and personal beliefs about when life begins, the removal of a transplanted uterus with a fetus could constitute loss of human life. There is also no way to quantify the emotional trauma that would be experienced by a recipient who lost both her transplanted uterus and her fetus, due to rejection.

Even when a uterine transplant is successful, the pregnancy experience is markedly different than a traditional pregnancy. A discussion of *normalcy* will come up in Chapter 3, and I feel the need to distinguish here that while (to many people) pregnancy is considered a normal part of a woman's life, no part of a UTx pregnancy is normal. It is extremely important for any potential uterine transplant recipients to be fully informed about the limitations of the procedure, so they do not elect to have the transplant because they believe that it will give them the complete pregnancy experience. During the uterine transplant, the recipient's fallopian tubes are not connected to the transplanted uterus, which means that a uterine transplant recipient will not be capable of becoming pregnant naturally. Recipients will, instead, undergo IVF. Since researchers are unsure if a donated uterus can support multiple births, only one embryo is implanted in the uterus per cycle. When there is

a successful IVF pregnancy, the gestational experience itself is also altered. The transplanted uterus does not have all of the nerves (because these nerves are not vital to the health of the uterus) and therefore women with transplanted uteri will not feel contractions in the traditional way. This lack of nerve connection also makes it harder for them to feel the fetal movement within the womb, including when the fetus kicks (Grady). Transplant recipients will always have their babies delivered via cesarean section, so there is no chance of a recipient experiencing vaginal birth (Maron, Donated Uterus). The children gestated in donated uteri will always be delivered slightly prematurely, so as to avoid fully stretching the uterus. Premature babies are more likely to have health issues than full term babies, so this added risk must be acknowledged.

The Montreal Criteria for the Ethical Feasibility of Uterine Transplantation provide a comprehensive list of criteria that the authors believe must be met in order for a uterine transplant to be ethically performed at this time. These criteria can serve as a good framework when moving forward with UTx clinical trials, but they are not equally accepted by all research teams and can be altered for better applicability. The Montreal Criteria specifically outline the different standards that must be met in order for a woman to be considered as a uterine transplant recipient or donor, and also provides a model to be followed by any healthcare team that wishes to perform this procedure. Some of the main guidelines are that the recipient must be a genetic female with a documented case of UFI, the donor must be a female of reproductive age who has repeatedly insisted that she desires the end of her fertility, and the health-care system must provide sufficient informed consent

to both parties (Lefkowitz et al 442-443). These criteria have not been strictly followed by all transplant teams, as the Swedish trial used several donors who were past reproductive age, but I believe that they provide a good indication of how UTx will be regulated in the future. Excerpts from the Montreal Criteria for the Ethical Feasibility of Uterine Transplantation are available in Appendix B.

Much of the debate over the ethics of uterine transplantation is due to the principles of autonomy and nonmaleficence. The principle of nonmaleficence is more colloquially stated in the Hippocratic Oath as "do no harm". While physicians vow not to bring harm to their patients (and performing a risky procedure like a uterine transplant for reasons that are not life-saving could be seen as constituting harm), the principle of autonomy would argue that a person should be able to make their own decisions about which risks they are willing to take.

In the case of the uterine transplant, according to The Montreal Criteria for the Ethical Feasibility of Uterine Transplantation, a woman's desire to reproduce and the right to reproductive self-determination (which is derived from the principle of autonomy) exerts an ethical obligation on the medical community to attempt to help her achieve her reproductive goals. Physicians involved in uterine transplantation are required to analyze the potential psychosocial benefits that can be obtained through UTx, and then compare them to the physical and emotional risks that a recipient would have to undertake in order to achieve those benefits (Lefkowitz et al 446). As in a normal cost-benefit analysis, if the psychosocial benefits outweigh the potential costs (risks), the procedure is deemed ethical. It is clear that in certain clinics, where these trials are underway, researchers, clinical trial administrators

and the IRB believe that all of the risks (which have been outlined in this chapter) can be mitigated by strict procedural guidelines and justified by the potential benefits that uterine transplants can bring to women with UFI.

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There are many circumstances that might arise if UTx is approved that I have not had time to discuss and analyze in this chapter. It is possible that a UTx recipient might refuse to have the donor uterus removed after childbirth, or that a patient might desire a uterine transplant but not wish to use that uterus for the purpose of gestation. It is also possible that a recipient might get pregnant and then desire an abortion. Each of these situations would raise questions about the ethicality of UTx, the purpose of the procedure and the autonomy of the women who would undergo transplantation. While these questions are important, they did not fit well into this specific thesis and I have not chosen to speculate about how the IRB would rule on these scenarios.

Chapter 3

Precedent for Quality-of-Life Procedures

While uterine transplants are currently experiencing bioethical scrutiny, the human uterine transplant is by no means the first medical procedure designed to address a health problem that is not strictly *life-threatening*. There are several other quality-of-life procedures that undergo, or have previously undergone, similar bioethical investigations. In this chapter, I have decided to examine hand, face and penile transplants. While all of these surgical operations can be considered "quality-of-life" procedures, there is a gradient of social acceptability that speaks to which physical qualities are more highly valued. Finally, it is largely important to identify and scrutinize the motivations for all of these procedures. We must determine if, and in which ways, these procedures improve the lives of the patients. If these quality-of-life procedures do not actually serve the purpose of bettering the lives of the individuals who undergo them, it could be true that they do more to serve the societal desire for uniformity than to serve the patient/recipient.

Quality-of-life transplants are not a new concept, and this is demonstrated by the legends and stories about limb and tissue transplants that have existed for over a thousand years. 'The legend of the black leg' (*Leggenda Aurea*) is an account of two twin brothers, Cosmas and Damian, who supposedly replaced the diseased leg of a sleeping man with a leg recovered from a dead Ethiopian Moor, in 348 CE. There are tales, also, of the father of modern plastic surgery, Gaspare Tagliacozzi, transplanting the nose of a slave to his master in the 16th century (Gander et al. 869). In the 1900s limb transplants, and even head transplants, were attempted on

animals and all of these studies helped to lay the groundwork for human allotransplantation. The first successful corneal transplant (a quality-of-life procedure to restore vision) was performed over 100 years ago in 1905 (Armitage 1222). Almost sixty years later the first hand transplant was attempted in Ecuador (unsuccessfully) and in 1999 a hand transplant was successfully performed on Clint Hallam, a New Zealander who had lost his hand in a prison accident. After the hand transplant, members of the medical community immediately set their sights on face transplants, and within six years the first partial face transplant was performed on the victim of a vicious dog attack. While these procedures are far from common, they have been accepted and mainly praised because they increase the quality-of-life of their recipients. The success of the face transplant has demonstrated the scope of possible transplant procedures and now researchers and surgeons are studying and attempting penile transplants.

At this point, over 85 patients have received hand or arm transplants at various different institutions around the world. The longest surviving hand/arm transplant is 11 years old and it belongs to the first US patient to receive one. Recipients of hand transplants must have had a below the shoulder amputation of one or both arms, or suffer from the severe deformity of one or both arm/hands. Even though these transplants have moved past the clinical trial stage, there are still strict parameters that a transplant recipient must meet, such as having no history of HIV or hepatitis C, being cancer free for at least five years, and a willingness to forgo pregnancy for one year. The recipient must also be older than 18 and younger than 65. This procedure is relatively low risk, but while Johns Hopkins Hospital states

"no patient taking his/her immunosuppression drugs on time and as advised has lost a transplanted hand/arm" (Lee, Hand/Arm), the clinic neglects to mention that post-operative non-adherence has, in many cases, been associated with rejection episodes, graft loss, and even death (Kumnig et al. 574). Often-times, the reasons for patient non-adherence stem from psychological issues, most notably identity problems that result from patients attempting to reconcile the fact that a piece of their body used to belong to someone else. In one case, a transplant recipient found out the identity of his organ donor, and was so upset by the situation that he committed suicide (Zhang et al. 798).

Even though, in addition to the matching of blood type and immunological parameters, the recipient/donor matching process involves an emphasis on matching skin color, skin texture, gender, ethnicity/race, and the size of the hand or arm, it is impossible to find a "perfect" physical match. The fact that the transplant will most likely be perceptibly different from the rest of the recipient's body is usually not a problem, but in some cases it can wreak emotional havoc. In order to avoid these identity problems as much as possible, it is important to psychologically evaluate potential transplant recipients, and look for warning signs of eventual non-compliance, such as premorbid psychiatric status, poor social support, substance abuse and pre-operative noncompliance (Kumnig et al. 574).

The potential loss of personal identity could be even more likely when considering face transplants, as the face is so strongly linked to one's personal sense of self. Since 2005, more than 20 patients have received full or partial face transplants at institutions around the world (Lee). Once again it seems that a face

transplant has yet to be fully rejected by a patient who complied with the post-operative regimen as set by the surgeons, and in this case, reports show that there has not been the same issue of noncompliance as seen with some of the hand transplant recipients (most notably Clint Hallam, who's hand was removed three years after the initial transplant). This difference could result from the fact that a face transplant does not make the recipient look like a photocopy of the donor. Instead, face transplant recipients will look neither exactly like their original selves nor like the donor. Due to the bone structure of the recipient under the donors face, they will have a composite identity (Freeman et al. 78). While face transplant recipients will surely need to adjust to their new identities, they can more easily reconcile their changed appearance because they are not simply taking the appearance of the dead donor.

"Penile transplantation shares similar considerations as face transplantation," says Dr. Redett of Johns Hopkins. "It involves a part of the body that is uniquely personal in nature and strongly associated with one's sense of self and identity as a male" (Pondrom, Penile Transplant 376). The penile transplant is a new procedure, though it has been desired by men who have lost their penises for decades. The surgery lasts 10 to 12 hours and involves the connection of a minimum of two nerves, two veins and four arteries. Similar to hand transplants, penile transplants do more than just replace a part of the body that is now missing. A successful penile transplant allows the recipient to gain an erection, perform penetrative sexual intercourse and ejaculate. Penile transplants and personal identity are strongly linked, but in contrast to hand and face transplants it seems that the penis

transplant is more likely to restore personal identity than to challenge it. While there will of course be the same struggle to find a "perfect match" to the recipient's skin tone and body type, the transplant will not be visible to society at large, so differences in those factors may not cause as big of a problem.

While all of the quality-of-life procedures that have been examined in this chapter have certain levels of risk, they have been approved, performed, and embraced (by many) in the United States. The fact that these surgeries exist sets a substantial precedent for uterine transplants, as they serve the same function and incur similar risks, all for the overarching goal of *perceived normality*.

I say that the general goal for all of these procedures is *perceived normality*, and that claim is based on my investigation into the motivations of each of these surgeries. According to interviews performed by Martin Kumnig and his colleagues, though the motivation for hand transplantation in bilateral amputees is mainly the need for increased function, when the patient has only lost one hand, the majority of their motivation stems from the desire to correct their "disturbed body image" (Kumnig et al. 574-576) and regain their original sense of psychological and social well-being. Researchers from Transplant International stated that many patients who have had hands amputated experience self-consciousness about their conspicuous physical differences from nonaffected people and as a result experience an increased level of shame when in public spaces (Kumnig et al. 575). By receiving the hand transplant, they can eliminate a level of perceptible physical difference and return to a state of near normality.

Similarly, at a press conference one year post-op, Mississippi firefighter Patrick Hardison, who underwent the world's most extensive face transplant, explained that the procedure has allowed him to walk down the street without people staring and children being frightened. Elated he explained, "I'm pretty much back to being a normal guy, doing normal activities"(Cha). Examinations into the ethicality of penile transplants also reveal a large focus on regaining normality. In an argument for penile transplants in the *Asian Journal of Andrology*, Li-Chao Zhang and her colleagues state that, "In a society that values 'normalcy' and rejects 'abnormality,' having a penile defect is not an insignificant matter." They go on to explain that the patients they spoke with "were commonly 'extremely concerned' about how their defect would affect their status in their family and in society" (Zhang et al. 796).

It seems that though these procedures are flouted as "quality-of-life", the main way that they increase that quality is to bring patients back into the realm of bodily normality, which has been set by societal standards. Though the process that is undergone to achieve these "fixed" physical appearances is rare and abnormal, in the end the recipient can be seen by others as looking "normal" as opposed to being deformed or lacking a part of their body. While this "normal is key" mentality is disturbing, it can be used to provide support for the "necessity" of uterine transplants because many societies, including the USA and Sweden, consider very few things to be more *normal*, or more acceptable, than a pregnant woman.

> As soon as I was visibly and clearly pregnant, I felt, for the first time in my adolescent and adult life, not-guilty. The atmosphere of approval in which I was bathed—even by strangers in the street, it seemed—was like an aura I carried with me, in which doubts, fears, misgivings, met with absolute denial. This is what women have always done. (Rich 26)

Uterine transplants are very much in demand, in fact, since the first successful uterine transplant in Sweden Dr. Brännström receives around 50 emails per day from women requesting the surgery. In addition to the requests, the emails usually include very heartfelt and sad personal narratives about why each individual "needs" the procedure (Pondrom, Uterus Transplants). In an interview discussing the negative psychological effects of UFI, Dr. Farrell proclaimed that, "Uterine Factor Infertility can have a profound impact on every aspect of a woman's life, from the time the diagnosis is made in adolescence onward," she says, "It affects how a woman views herself and enters relationships." She went on to explain that this negative impact is reason enough to justify UTx, "It's not lifesaving, but it can be life-altering" (Ethical Considerations Paramount in Uterine Transplant). Dr. Brännström echoed this sentiment as he discussed the experiences of his patients post-UTx, "Some of them are 30 or 32 and they've never had a period before, and they think it's so fantastic," he stated. "They say, 'Now I feel like a real woman'" (Medew and Orange).

What proponents of UTx typically tend to gloss over is the fact that women are so adversely affected by UFI, hysterectomies, and infertility as a whole, because of the pressure to conceive naturally. Women are taught at a very young age that their anatomy defines them. "Women" have vaginas and uteri and because of those physical attributes they have the ability to gestate children, give birth to them and then nourish them with breast milk. Not only are they able to do those things, but they are expected to, because the most womanly thing an individual can do is carry a child and become a mother. This rhetoric also equates womanhood with fertility,

because a girl does not "become a woman" until she begins menstruating, and to some, you are not a *real* woman until you are a mother, or on the path to achieving motherhood.

> "In the experience of the pregnant woman, this weight and materiality often produce a sense of power, solidity, and validity. Thus, whereas our society often devalues and trivializes women, regards women as weak and dainty, the pregnant woman can gain a certain sense of self-respect" (Young 53).

It makes sense that women would believe that the lack of a uterus, and therefore the inability to achieve the type of self-respect that Iris Young describes in the quote above, would lower their quality-of-life. By going under the knife and receiving a donated uterus, an "abnormal" woman can reclaim, or claim for the very first time, her normalcy. Though this glorification of "normal bodies" and the value placed on gender roles in society are both destructive forces in the lives of women (and people of all identities), they have a very real impact on quality-of-life. Since women are forced to live within a society that idolizes normality and pregnancy, they should have access to UTx because it will help them gain a social power that they have been denied, even if that power is only temporary.

While all three of the previously mentioned transplants (hand, face and penis), are quality-of-life procedures, they have extremely different levels of surgical and ethical complexity and tend to involve differing levels of physical and emotional risk. Though uterine transplants are also quality-of-life transplants they stand apart from the others for multiple reasons, but the most important one might be that they don't require a dead donor. Though some clinical trials (like the Cleveland Clinic) are using cadaver uteri, the only successful uterine transplants have come from

living donors. All quality-of-life transplants involve the recipient taking on surgical risk for non-life-saving reasons, but UTx is the only one thus far that also involves a live donor incurring risk. While the other procedures I have described are permanent, uterine transplants are designed to be temporary. Additionally, while face and hand transplants are visible to anyone who comes in contact with the recipient (and penile transplants can be visually detected by individuals who engage in sexual relations with the recipients), no one can see a uterine transplant. In this way, UTx might be considered more similar to a kidney or liver transplant than to a hand/face/penis transplant. Due to these differences, the justification for the uterine transplants clearly must be different, but that does not mean that the justification is not valid.

Chapter 4

Moving Forward with UTx

I have examined the ethical dilemmas associated with uterine transplantation and discussed them within the context of other assisted reproductive technologies and quality-of-life procedures. While I find it clear that there are ethical issues with uterine transplantation (including mental and physical risk to the fetus and mother, accessibility, and the altered gestational experience), the procedure offers more possible benefits than risks, for those who might seek it out. When the medical community generally accepted non-life-saving transplants, such as hand and face transplants, it set a precedent for other quality-of-life procedures, including UTx. First-hand accounts from UTx recipients like Emelie Eriksson, the first woman to give birth to a uterine transplant baby, and even Lindsay McFarland (who experienced a failed transplant) are extremely positive about the procedure and both women have expressed the desire to see the UTx become available for "everyone that needs it" (Larsson).

Due to the fact that UTx has been successfully performed, widely sought out, and considered ethical by multiple hospital Institutional Review Boards (IRBs), I believe that uterine transplantation will be approved, and become a part of the American medical system, within a decade. While it is easy to foresee a future for UTx, it is difficult to conceptualize the path that uterine transplantation will follow if or when it moves past the clinical trial phase. Currently there are active trials using live donors (Baylor) and dead donors (Cleveland Clinic) and there is also the potential

option of 3D printed uteri, which would eliminate the need for human donors all together.

At this point, there has been no official success with the use of uteri harvested from dead donors. I believe that if there is no change in this trend, the medical community will move forward with a transplantation model revolving around live donors. In this case, it will be extremely important to establish strict guidelines for achieving informed consent by the donors. All potential uterine donors will need to understand the possible risks to their physical and mental well-being. Donors must also be acutely aware of the fact that the procedure is irreversible and that they will never be able to gestate again. Finally, it will be imperative for all donors to understand that upon donation they give up all rights to the organ. The donor must know that they will not be a genetic contributor to, or have legal claim to, any resulting children. There will also have to be different protocols for living unrelated donors and living related donors.

The issue of informed consent will also arise if uterine transplantation from dead donors proves to be viable. In the trials at the Cleveland Clinic, uteri are being retrieved from organ donors whose family members specifically approved the donation of the uterus (Grady). This was deemed acceptable by the IRB in the case of the Cleveland trial, but the system is problematic because there is no way to be certain that the dead donor would have approved of the donation of her uterus. As Arthur Caplan and his colleagues mentioned in *Moving the Womb*, their 2007 warning against uterine transplantation, very few women who consent to be organ donors ever imagine that their uterus could be one of the organs transplanted into a

recipient (Caplan, 19). Currently, when registering as an organ donor, an individual is able to pick and choose which organs they feel comfortable donating after death (HRSA). If uteri are going to be harvested from dead donors, they will need to be added to the organ donor registry in order to ensure that organ donors are made aware of the potential removal and donation of their uteri before they die.

In June of 2016 The United Network for Organ Sharing (UNOS) transplant board approved the incorporation of uterine transplants, along with seven other Vascularized Composite Allograft transplants, into their registry (Levin & Wholley). Currently there are 6 uterine transplants on the *Transplants by Organ Type January 1, 1988 - March 31, 2017* list and there is one transplant candidate on the waiting list (Data | UNOS). While UNOS has been quick to cover this new procedure, the organization has yet to publish UTx-specific guidelines for the allocation of transplants. Uterine transplantation does not fit into the traditional UNOS allocation system—which numerically ranks transplant candidates, often considering length and severity of illness and life expectancy without the transplant. With non-life-saving transplants like uterine, face and hand transplants the allocation list will have to be organized differently, most-likely culminating in a system where all transplant candidates who are compatible with the donor (due to blood type and other medical factors) are put on a list and then the transplants are distributed on a first-come first-serve basis.

While current research into UTx will surely be aided by either deceased donation or live donation (or some combination of the two), the promising work on 3D organ printing may one day become applicable to the UTx process. Currently, 3D

models of organs can be printed to aid in educational demonstrations and to allow surgeons to rehearse difficult procedures, but experts expect that it could be decades before 3D bioprinting (using a bioink composed of tissue or human cells to produce functioning body parts) progresses enough to develop fully functioning organs (Pondrom, 3D Printing 1339). If full-organ bioprinting is ever achieved, uterine transplantation could be practiced without the use of a donor, deceased or living, and the organ would be perfectly tailored to the recipient. While bioprinting is also bioethically complicated, this application could combat many of the perceived issues with uterine transplantation (risk for the donor, the necessity of immunosuppressant drugs while gestating, and the eventual removal of the transplant).

In addition to future changes in the way that donor uteri will be procured, it is very possible that the pool of UTx recipients will also expand in the coming years. While modern research is focused on cis-women who lack uteri, a strong interest in uterine transplants has been expressed by trans communities, and many researchers are already considering bring trans individuals into the fold. While it is difficult to find academic literature discussing UTx in trans patients, social networking forums like Tumblr and Reddit, as well as popular media websites such as the Huffington Post, have discussed this possibility. When approached, several researchers have postulated that it will be possible to perform uterine transplantation on trans-women within the next two decades. Some professionals are even more optimistic. In November of 2015 Dr. Karine Chung, director of the fertility preservation program at the University of Southern California's Keck School

of Medicine, stated that the procedure would be possible within five to ten years (Gordon).

The lag-time between trials with cis-females and trials with trans-women is caused both by moral and practical reasons. Theorists like John Robertson and Amel Alghrani strongly support UTx for genetic females because they believe that these women have the "right to gestate". They do not, however, believe in trans-inclusive UTx because that "right to gestate" does not extend to trans-women and cis-men. UTx for cis-women can be considered "designed to restore natural function" (Alghrani 638) where as, in trans-women it would allow a fertility function that was not naturally intended. These moral judgments may significantly impact the future of trans-UTx, but the most important factor impeding research into trans-UTx at this moment is that the anatomy of a male-to-female (MTF) patient is not nearly as conducive to uterine transplantation as the anatomy of a genetic female.

In order for a MTF trans patient to receive a uterine transplant, they would first need castration surgery and high doses of exogenous hormones to combat their natural androgens (which, if left at their natal levels, could threaten pregnancy). They would also need to have a neovagina created (if they didn't already have one) to allow for menstruation and the eventual implantation of embryos (Maron, Transgender). Additionally, while the majority of genetic females who lack uteri still have most, if not all, of the internal structures necessary to support the uterus, genetic males lack the uterine veins and arteries needed to nurture the womb. Though it will be more difficult, Dr. Chung has proposed attaching a branch of a large vessel, like the internal iliac, to the donor uterus upon transplantation

(Gordon). If UTx in genetic females proves to be viable, I predict that research into trans-UTx will quickly follow. While the process will be more complicated, there is a vast network of people who would be willing to undergo uterine transplantation in order to achieve this level of reproductive autonomy.

At this moment, while UNOS has accepted cis-gendered uterine transplantation, there is no way to know how trans-UTx might be dealt with by the network. Mark Sauer, professor of obstetrics and gynecology at Columbia University, and a member of The American Society for Reproductive Medicine's Ethics Committee, disclosed that while the board has started discussions about the potential prioritization and allocation of uterine transplants, trans-recipients have not been a part of the conversation (Maron, Transgender). The erasure of trans individuals from this discussion may foreshadow uneven allocation trends if there does come a time where both cis and trans individuals are on waiting lists for donor uteri. It is not unreasonable to fear that genetic sex may one day constitute a variable in the allocation process of uterine transplants, with genetic females being afforded a higher level of priority.

One factor that would help trans-UTx immensely is that female-to-male (FTM) patients are often more than willing to part with their uteri. Cecile Unger, a specialist in female pelvic medicine at the Cleveland Clinic, has stated that around one third of her female-to-male patients have requested to donate their uteri for transplantation (Maron, Transgender). At this point, these requests are being denied, but if there comes a time where trans-UTx is in clinical trials or readily available, there will probably be no shortage of donor uteri from FTM patients.

While some of these uteri may be regulated by UNOS, it might also be possible to create a trans-network of organ sharing. While this system could definitely work on a more individual level, with trans men donating their uteri to MTF friends or family members, it could also be regulated on a grander scale by an online system capable of matching trans recipients with biologically compatible trans donors.

As more patients seek the benefits of UTx, the question of payment will arise. Even now, many insurance companies do not cover assisted reproductive technologies like IVF, and if they do, they often only cover one or two cycles. Uterine transplants will be much more expensive, as they have an estimated cost of up to $300,000 (Hastings Center) and will require lengthy hospital stays for both the donor and the recipient. It is unlikely that insurance companies will be quick to cover this procedure. If these procedures are not incorporated into insurance packages, uterine transplants are sure to follow the same path as the more established ARTs—where they are available to the privileged upper class and remain unreachable by middle and lower class individuals who could greatly benefit from them. The issue of payment will be specifically glaring for trans-patients, as many trans-men and women already struggle to afford hormone treatments and top/bottom surgeries. While certain insurance plans do cover gender reassignment surgeries, there are specific qualifications that must be met in order for the surgery to be deemed "medically necessary" and all procedures considered to be cosmetic are excluded from coverage (HRC). It is possible that some providers might one day consider UTx to be a necessary part of the reassignment process, but it is more likely that it will be considered cosmetic and remain largely unattainable.

One indisputable aspect of the future of UTx is that uterine transplant babies will be closely observed over the next decade. While, at this point, researchers believe that children gestated in UTx uteri have not been, and will not be, negatively affected by this form of gestation, more time and a larger sample size will be required before they can make concrete claims. Caplan has suggested that, once the current clinical trials are finished, the medical community take a few years to track a small group of UTx recipients and their children. This way, they might be able to gauge how the transplant affects the health and development of UTx babies before the procedure becomes more widely available (Tedeschi). Though this seems like a practical tactic, urging from potential UTx patients coupled with the desire to provide this cutting edge procedure might prompt certain hospitals to forego the waiting period and offer UTx as soon as possible.

If UTx moves past clinical trails and becomes a part of the American medical system, reproduction in this country will be forever changed. Moreover, if trans-UTx is actualized, or if bioprinting becomes a viable source of transplantable uteri, reproduction and gestation will reach a new level of unnatural. It is imperative that we acknowledge that each step forward in UTx takes us farther away from the traditional systems of reproduction and gestation. Whether this potential departure from natural gestation is positive or negative is not the focus of this thesis, but there will surely be strong arguments for both sides if UTx research progresses.

Conclusion

Uterine transplantation, while imagined and discussed for centuries, became corporeal when Lili Elbe went under the knife in 1931. Decades later, it seems that UTx may become an integral part of the future of assisted reproductive technologies. Uterine transplantation has now been attempted in three official human clinical trials and many more animal studies and there are currently 5 children in Sweden who were gestated in donor uteri. When looking at the path that this procedure has followed, it seems evident to me that UTx is on track to gain approval in several countries (including the US, Sweden and Great Britain).

Throughout this thesis I have demonstrated the bioethical problems associated with uterine transplantation. I have also indicated that it is a controversial issue; with certain bioethicists strongly opposing its progression, and others praising the procedure for aiding female procreative liberty. While the ethical issues associated with UTx may seem potentially prohibitive, it is necessary to acknowledge that all current medical procedures (ranging from IVF to kidney transplants) are associated with certain bioethical issues. Therefore, an examination into the specific ethical problems and the counteracting benefits must be conducted before any new medical or scientific technique is approved. I have attempted to perform an abbreviated version of this assessment for UTx and have come to the conclusion that, while the progression of uterine transplantation should be cautious and highly regulated, it should continue, due to the fact that this procedure has the potential to provide immeasurable quality-of-life benefits to individuals who lack uteri.

While I don't think that UTx will ever become "common practice", I believe it should be available for the specific individuals who, after being fully informed, consent to undergo the procedure. The multiple procedures required in order to attain a uterus, and subsequently gestate a fetus, may not seem "worth it" to an outsider, but it is impossible to quantify the desire felt by these individuals. Since UTx provides an opportunity that is not made available by any pre-existing medical technology, I consider it to pass clinical equipoise and be justifiable.

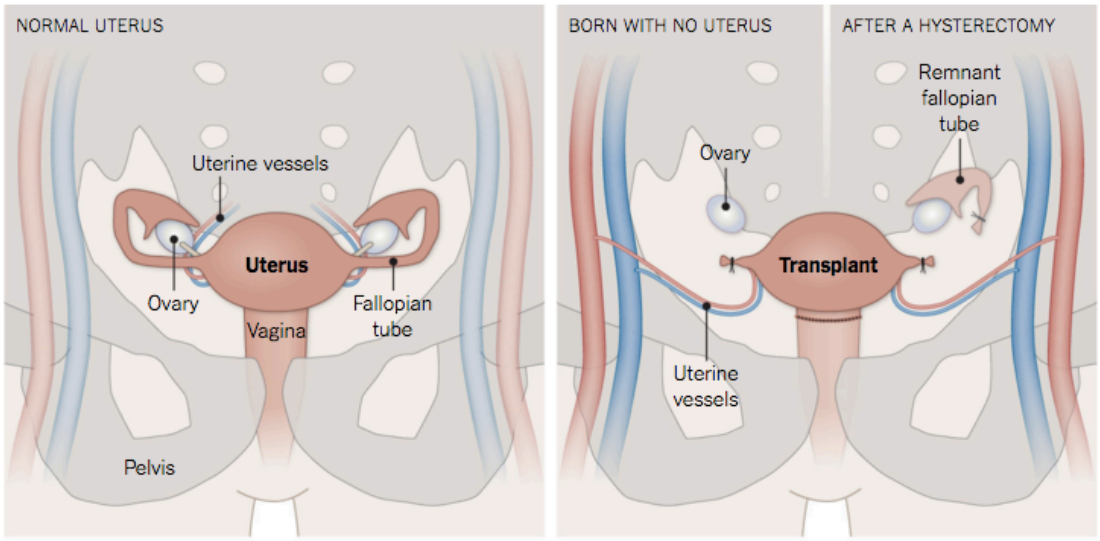
However, before uterine transplantation graduates from clinical trials and becomes mainstream, a variety of regulations will need to be nailed down. I hope to see the establishment of strict qualifications for all potential UTx recipients, outlined procedures for procurement of uteri from live and dead donors, and guidelines for how to deal with any malfunctions that may occur during the procedure and the subsequent gestational period. It will also be necessary for UNOS to publish specific allocation policies regarding uteri. Finally, it will be interesting to see the future of this procedure in terms of payment, as most insurance providers will probably resist incorporating the expensive and rare procedure into their policies.

Uterine transplantation has the opportunity to change the face of human reproduction in a similar way to IVF, the procedure that revolutionized the field of assisted reproductive technologies in the late 1970s. Transcending the reach of traditional IVF, UTx might also allow procreation and gestation to become more accessible to gender-bending members of society, such as trans-women and cis-men who desire the experience of pregnancy. UTx, for the first time in history, is giving individuals who lack uteri the opportunity to achieve reproductive success in the

form of pregnancy and childbirth. While it is essential to acknowledge and mitigate the bioethical issues associated with UTx, they are not grave enough to derail this progress.

Appendix A

Human Uterine Transplant Model



THE DONOR Surgeons remove the uterus, cervix and part of the vagina from an organ donor who has recently died, along with the small uterine vessels that carry blood to the organ. The uterus can survive outside the body for at least six to eight hours if kept cold.

THE RECIPIENT The donor's uterus is connected to the recipient's vagina and the uterine vessels are redirected to large blood vessels running outside the pelvis. The recipient's ovaries are left in place, and if she has any remnant fallopian tubes, they are not connected to the transplant. The recipient will wait a year to heal before having in vitro fertilization.

Source:
Grady, Denise. "Uterus Transplants May Soon Help Some Infertile Women in the U.S. Become Pregnant." *New York Times*. The New York Times Company, 12 Nov. 2015. Web.

Appendix B

Excerpt –*The Montreal Criteria for the Ethical Feasibility of Uterine Transplantation*

1. Criteria for the Ethical Feasibility of UTx

Assuming that a human uterine transplant is shown to lead to a viable gestation and is proven to be medically safe for the mother and fetus, a woman may be considered as a candidate for a uterine transplant if and only if all of the following criteria, as they pertain to three distinct groups, are met:

1. The recipient
    a. is a genetic female of reproductive age with no medical contraindications to transplantation,
    b. has documented congenital or acquired UFI which has failed all current gold standard and conservative therapy,
    c. (**c1**) has a personal or legal contraindication to surrogacy and adoption measures, or (**c2**) seeks the UTx solely as a measure to experience gestation, with an understanding of the limitations provided by the UTx in this respect,
    d. has not had her decision to undergo UTx deemed as irrational expert psychological evaluation,
    e. does not exhibit frank unsuitability for motherhood, and
    f. is responsible enough to consent, informed enough to make a responsible decision, and not under coercion.

2. The donor
    g. is a female of reproductive age with no medical contraindications to donation,
    h. (**h1**) has repeatedly attested to her conclusion of parity, or (**h2**) has signed an advanced directive for post-mortem organ donation,
    i. has no history of uterine damage or disease, and
    j. is responsible enough to consent, informed enough to make a responsible decision, and not under coercion.

3. The health care team
    k. is part of an institution that meets Moore's third criteria as it pertains to institutional stability,
    l. has provided adequate informed consent to both parties regarding risks, potential sequelae, and chances of success and failure,
    m. has no conflict of interest independently or with either party, and
    n. has the duty to preserve anonymity if the donor or recipient do not explicitly waive this right.

Source:
Lefkowitz, Ariel, Marcel Edwards, and Jacques Balayla. "The Montreal Criteria for the Ethical Feasibility of Uterine Transplantation." *Transplant International* 25.4 (2012): 444. Web.

2. Ethical Principles and Uterine Transplantation

Against UTx:

Principle of non-maleficence

- requires persons to refrain from causing others harm
- opposes UTx, as UTx involves bodily and potentially psychological harm of recipients and donors
- encourages extensive research of potential risks to the donor, recipient, and fetus
- promotes stringent medical and psychological evaluation of UTx candidates prior to approval

In favour of UTx:

Principle of autonomy

- asserts the right of persons to make their own choices, and mandates that others respect these choices
- the principle of autonomy gives rise to the right to self-determination, including in the dominion of one's body
- supports UTx, as UTx performed in the context of proper informed consent respects the donor and recipient's right to govern their own bodies and reproductive potential

Equivocal regarding UTx:

Principle of beneficence:

- encourages persons to do good for others
- depends on the particular instance of UTx (the specific donor, recipient, and health care team)
    - if the Montreal Criteria are met, then the authors of this paper believe that the UTx does more good than harm
    - if the criteria are not met, then the authors believe that UTx would be unacceptably harmful

Principle of justice:

- promotes the equality of persons, the right to equal access to opportunities offered and the right to be given one's due
- requires that the participants of clinical trials be part of the population that will benefit from the research
- recommends that UTx be offered to all appropriate candidates, if it is found to be safe and effective

Source:
Lefkowitz, Ariel, Marcel Edwards, and Jacques Balayla. "The Montreal Criteria for the Ethical Feasibility of Uterine Transplantation." *Transplant International* 25.4 (2012): 445. Web.

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